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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
TRAVERS, RUSSELL S	
ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 08/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/881,213	SANDBERG ET AL.	
	Examiner	Art Unit	
	Russell Travers, J.D.,Ph.D	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,9-11 and 21-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,9-11 and 21-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

The amendment filed June 30, 2004 has been received and entered into the file.

Applicant's arguments filed June 30, 2004 have been fully considered but they are not deemed to be persuasive.

Claims 1-7, 9-11 and 21-24 are presented for examination.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to adequately teach how to make and/or use the invention, and thereby failing to provide an enabling disclosure.

The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,

2) the amount of direction or guidance provided,

3) the presence of absence of working examples,

4) the nature of the invention,

5) the state of the prior art,

6) the relative skill of those in the art

7) the predictability of the art, and

8) the breadth of the claims.

Applicant fails to set forth the criteria that defines "natural biotin", "linkers", a "trifunctional crosslinking moiety" or avidin of strepavidin "derivatives of fragments thereof having essentially the same binding function to biotin as avidin or streptavidin" useful for practicing the invention as claimed. Additionally, Applicant fails to provide information allowing the skilled artisan to ascertain these compounds without undue experimentation. In the instant case, only a limited number of "natural biotin" compounds, "linkers" compounds, a "trifunctional crosslinking moiety" compounds or avidin of streptavidin "derivatives of fragments thereof having essentially the same binding function to biotin as avidin or streptavidin" useful for practicing the invention as claimed examples are set forth, thereby failing to provide sufficient working examples. It is noted that these examples are neither exhaustive, nor define the class of compounds required. The pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. The instant claims read on all "natural biotin" compounds, "linkers" compounds, a "trifunctional crosslinking moiety" compounds or avidin of strepavidin "derivatives of fragments thereof having essentially the same binding function to biotin as avidin or streptavidin" useful for practicing the

invention as claimed, necessitating an exhaustive search for the embodiments suitable to practice the claimed invention. Applicants fail to provide information sufficient to practice the claimed invention, absent undue experimentation.

Claims 1-7, 9, 21, 23 and 24 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

Claims 1-7, 9, 21 23 and 24 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-7, 9, 21, 23 and 24 are rendered indefinite by the terms and phrases "natural biotin" compounds, "linkers" compounds, a "trifunctional crosslinking moiety" compounds or avidin of strepavidin "derivatives of fragments thereof having essentially the same binding function to biotin as avidin or streptavidin" and thereby failing to clearly set forth the metes and bounds of the patent protection desired. Criteria defining medicaments that are "natural biotin" compounds, "linkers" compounds, a "trifunctional crosslinking moiety" compounds or avidin of strepavidin "derivatives of fragments thereof having essentially the same binding function to biotin as avidin or streptavidin" useful for practicing the invention as claimed are not set forth in the specification, thereby failing to provide information defining the instant inventions metes and bounds. Applicant's term fails to clearly define the subject matter encompassed by the instant claims, thus is properly rejected under 35 USC 112, second paragraph.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-7, 9, 21, 23 and 24 are rejected under 35 U.S.C. § 102(b) as being anticipated by Wilber et al.

Wilber et al teach the instant linking compounds as containing biotin, tri-functional linking compounds (see page 39 and page 44, line 25), as useful for binding to streptavidin with those linkers and tri-functional compounds herein envisioned (see page 65, example 14). Examiner notes the prior art compounds taught by Wilber et al are useful in-vivo and in-vitro, indistinguishable from the extra corporeal use herein claimed.

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains.

Patentability shall not be negatived by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

Claims 1-7, 9-11 and 21-24 are rejected under 35 U.S.C. § 103 as being unpatentable over Norrgren et al and Chen et al in view of Wilbur et al.

Norrgren et al and Chen et al teach the use of extracorporeal methods for providing and enhancing various therapeutic regimens, to include radio nuclide anti-cancer therapy. Norrgren et al and Chen et al teach the useful nature of extracorporeal extraction of various toxic medicaments, bound and unbound, employing various specific adsorption columns (see Norrgren et al figure 1). Chen et al teach the desirability of extracorporeal extraction via immunoadsorption for various therapeutic regimens (see figure 3). Wilber et al teach the claimed trifunctional linkers as old and well known in combination with various specific therapeutic functional moieties, as herein claimed (see page 20, paragraph 2). These medicaments are taught as useful for adsorbing to a column for extracting various compounds (see page 2, lines 1-2. Claims 1-7, 9-11 and 21-24 and the primary references, differ as to:

1) the specific recitation of the prior art trifunctional linkers for loading extracorporeal columns, and

2) those specific linker lengths herein claimed.

As stated above, Wilber et al teach the instant trifunctional linking compounds as useful for adsorbing to a column for extracting various compounds (see page 2, lines 1-2). Norrgren et al teach the useful nature of extracorporeal extraction of various toxic medicaments, bound and unbound, employing various specific adsorption columns (see Norrgren et al figure 1). In figure 1, Norrgren et al illustrate the use of a column with specific adsorbed linkers for removing toxic medicaments extra corporeally, as herein claimed. This teaching would have motivated the skilled artisan to employ various linking agents, such as those taught by Wilber et al, in removing toxic agents extra corporeally. Attention is directed to Wilber et al teaching problems of stearic hindrance with employing various linking compounds; with these hindrance problems overcome with those linkers disclosed by Wilber et al (see pages 38-40) motivating the skilled artisan to employ those linkers taught by Wilber et al. Stearic hindrance is taught by Wilber et al as reduced by his linking agents (see compounds 46 and 48), and with the ideal linker chain length being 20-60 angstroms (see page 29). Possessing the Examiner cited prior art, the skilled artisan would have been motivated to employ extracorporeal extraction of toxins associated with therapeutic regimens. Wilber et al teach the instant trifunctional linking agents as old and well known for linking the claimed various specific therapeutic functional moieties, as herein claimed (see page 20, paragraph 2). It is generally considered prima facie obvious to combine two compounds each of which is taught by the prior art to be useful for the same purpose, in order to form a composition which is to be used for the very same purpose. The idea

for combining them flows logically from their having been used individually in the prior art. As shown by the recited teachings, the instant claims define nothing more than the concomitant use of conventional botin based linking compounds. It would follow that the recited claims define prima facie obvious subject matter. Cf. In re Kerhoven, 626 F.2d 848, 205 USPQ 1069 (CCPA 1980). The skilled artisan possessing the Examiner cited teachings would have seen trifunctional linking compositions, and the administration of these compounds to columns for extracorporeal extraction of therapeutic toxins as residing in the skilled artisan purview.

RESPONSE TO ARGUMENTS

Those rebuttal arguments that aver a very improved stability are not based on a claimed limitation. That rebuttal arguments based on unclaimed limitations are moot is well settled patent law. Examiner additionally notes the instant claims are not illustrated as possessing unexpected stability in the instant specification.

Examiner notes the specific employment of a chromomatographic device is not recited in the instant claims. The recitation of in-vitro (see page 17, line 21) meets the extra-corporeal limitation herein argued.

That rebuttal argument presented a page 13 (paper filed June 30, 2004) avers a teaching away; a teaching away is not presented by Wilber et al. To teach away, the prior art must specifically direct the skilled artisan from employing the claimed invention. In the instant case, Wilber et al is simply reciting a specific use for the numerous embodiments taught by Wilber et al.

Those rebuttal arguments with regard to specific bond lengths, and other functional limitations are unconvincing. Attention is directed to Wilber et al teaching the individual ingredients herein envisioned as useful for producing biotin binding molecules useful for the utility herein envisioned. As set forth above, Wilber et al teach the instant linking compounds as containing biotin, tri-functional linking compounds (see page 39 and page 44, line 25), as useful for binding to streptavidin with those linkers and tri-functional compounds herein envisioned (see page 65,example 14). Examiner notes the prior art compounds taught by Wilber et al are useful in-vivo and in-vitro, indistinguishable from the extra corporeal use herein claimed.

Attention is directed to Wilber et al teaching trifunctional compounds to effect "extracorporeal immunoabsorptive removal methods" indistinguishable from those herein claimed. Simple perusal of the Wilbur et al publication supplies the skilled artisan with those ingredients to practice the invention as claimed. Failure of Wilbur et al to specifically disclose those compounds herein claimed, precludes anticipation by Wilbur et al, but has little effect on this patent□s powers of obviation. Those specific linking agents envisioned by Applicants are disclosed at page 11 (see Wilbur et al page 1, examples 1-8, especially no. 1). At page 14, Wilbur et al teach those core moieties herein envisioned as useful for the extracorporeal use claimed herein (see page 14, example 30). Although Wilbur et al fails to recite the linker arm length herein disclosed, guidance is provided to reach those compounds envisioned by Applicants. At page 15, Wilbur et al teach a minimum are length of 9 angstroms, with a preferred length of 6-20 atoms encompassing those arm lengths set forth in the instant claims. Additionally,

Wilbur et al teach ether linkages, as employed by Applicants, as beneficial to "aid in the water solubilization of the Biotin moiety" (see page 15, paragraph 2).

Applicants aver unexpected benefits residing in the claimed subject matter, yet fail to fails to set forth evidence substantiating this belief. Evidence as to unexpected benefits must be "clear and convincing" *In re Lohr*, 137 USPQ 548 (CCPA 1963), and be of a scope reasonably commensurate with the scope of the subject matter claimed, *In re Linder*, 173 USPQ 356 (CCPA 1972). The data provided by Applicants is neither clear, convincing, nor reasonably commensurate in scope with the instant claims. Absent claims commensurate with the showing of unexpected benefits, or a showing reasonably commensurate with the instant claims, such claims remain properly rejected under 35 USC 103.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Travers, J.D.,Ph.D whose telephone number is 571-272-0631. The examiner can normally be reached on Monday to Thursday from 7:00 to 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Art Unit 1617